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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,048	EL-NAGGAR ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,15 and 18-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13,15 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed December 06, 2005, claims 10 and 18 have been amended; claims 1, 8 and 16 have been canceled; and claims 23 and 24 have been newly added.

2. Claims 10-13, 15, 18-24 are currently pending for prosecution on the merits.

Summary of Action

3. The rejection of claims 1, 8 and 16 under 35 U.S.C. 102(a) as being anticipated by Greenberg et al. (Journal of Clinical Pharmacology, 2000, 40 (12, Pt2), pp. 1509-1515) is not maintained in light of the amendment.

4. The rejection of claims 5, 9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenberg et al. (The Journal of Clinical Pharmacology, 2000, 40 (12, Pt.2), pp. 1509-1515), and further in view of Burch et al. (US 6552031) and Drug Facts and Comparison (1995 Edition, pp. 1248) is not maintained in light of the amendment.

5. The rejection of claims 10-13, 15, 18-22 under 35 U.S.C. 103(a) as being unpatentable over Lai et al. (US 6306842 B1) in view of Ares et al. (US 5399584), and further in view of Shapiro (US 6444221) and Drug Facts and Comparison (1995 Edition, pp. 1248) is not maintained in light of the amendment.

6. Applicant's amendment requiring "concurrently" in claim 10 and "the low dose aspirin is not covalently attached to the COX2 inhibitor" in claims 23-24 necessitates a new ground of rejection in this Office Action.

Response to Arguments

7. Applicant's arguments with respect to the claims1, 5 and 8-22 have been considered but are moot in view of the new ground(s) of rejection.

New Matter

8. The amendment filed December 06, 2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "the low dose aspirin is not covalently attached to the COX2 inhibitor".

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 23-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims in this application introduce negative limitation as discussed in preceding comments, namely "the low dose aspirin is not covalently attached to the COX2 inhibitor". The examiner determines that when all evidences in the original disclosure are considered and carefully reviewed, the newly added claims fail to find support in the original specification.

The specification discloses a combination of (i) standard doses of COX-2 inhibitor, (ii) aspirin at doses ranging from 70-350mg and/or (iii) antioxidant (i.e., flavanoids, flavonoids or isoflavones) that is useful for the treatment of inflammatory disorders, cancer and thrombosis, wherein said combination is prepared in various dosage forms including gelatin capsules, tablets and suspension (page 5, line 8 thru page 8, line 18). The specification discloses that the combined compounds of the invention may be formulated in single dosage form. Alternatively when not formulated together in a single dosage unit, an individual COX2 inhibitor may be administered at the same time as either aspirin or antioxidants or sequentially, in any order thereof (page 8, lines 21-28).

As stated above, the specification only positively states about the boundaries of the claim. There is no express statement about the negative limitation that can be found in the specification. Thus, the exclusion of said elements implies the inclusion of all other elements not expressly excluded, clearly illustrating that such negative limitations do, in fact, introduce new matter. The negative limitation recited in the present claims, which did not appear in the specification filed, introduces new concepts and violate the description requirement of the first paragraph of 35 USC 112.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Dependent claim 11 further limits the subject matter of a previous claim 14 which was canceled. Thus, Claim 11 is vague and unclear and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

For the examination purpose, claim 15 is understood as being dependent on the independent claim 10.

Claim 15 recites that the therapeutic composition prepared in "an enteric coated formulation". It appears in view of the independent claim 10 that each of active ingredients of the invention is administered concurrently to the patient. In other words, said therapeutic composition is not formulated together in a single dosage unit. Since the claimed "enteric coated formulation" can be formulated when the composition is prepared in a single dosage unit, the applicant's failure to further limit the subject matter of the previous claim leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 10-13, 18-21 and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hedden et al. (WO 01/45705) in view of Langhoff (DE 19855426 A1) and Shapiro (US 6444221).

Hedden teaches the use of COX-2 inhibitor such as celecoxib and rofecoxib for the treatment of inflammatory disorders including arthritis (page 2, line 16; page 3, line 6; page 19, lines 10-12).

Langhoff teaches the use of low dose aspirin(in dosage range of 30mg-75mg) for the treatment of anti-inflammatory disorder including rheumatism and arthritis.

Shapiro (US 6444221) teaches the use of flavonoids, flavanoids and isoflavones (i.e., daidzin, genistein, quercetin, silymarin, etc...) as antioxidants having functional equivalent property for the treatment of inflammatory disease conditions including arthritis or rhuematoidal arthritis (column 9, line 52 thru column 10, line 32; column 20, line 47 thru column 21, line 8).

The teaching of Hedden differs from the claimed invention in combination use of said COX-2 inhibitor, low dose aspirin and flavanoids or isoflavones. To incorporate such teaching into the teaching of Hedden, would have been obvious in view of Langhoff who teaches the use of the low dose aspirin for the treatment of arthritis and Shaprio who teaches the use of flavonoids or flavones for inflammatory condition including arthritis.

Above references in combination make clear that COX-2 inhibitor such as rofecoxib and celecoxib, low-dose aspirin and antioxidants (i.e., flavanoid, flavonoid and isoflavone) have been individually used for the treatment of arthritis. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).*

With respect to the claimed concurrent administration, those of ordinary skill in the art would have been readily optimized concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient. Determination of the appropriate administration regimen for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of

tasks routinely performed by them without undue experimentation, in absence evidence to the contrary.

12. Claims 15 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hedden et al. (WO 01/45705) in view of Langhoff (DE 19855426 A1) and Shapiro (US 6444221), and further in view of Burch et al. (US 6552031) and Drug Facts and Comparison (1995 Edition, pp. 1248) and Hendeler (US 6541613B2).

The modified teaching of Hedden includes all that is recited in claims 15 and 22 except the preparation of said combination in an enteric-coated formulation.

Burch and Drug Facts and Comparison being supplied as a reference to demonstrate the art recognized skill in preparing rofecoxib, low dose aspirin or antioxidants (i.e., isoflavones) in enteric coating formulation (see column 18, line 31 thru column 23, line 3 of Burch; commercially available Bayer Low Adult Strength 81mg in Facts and Comparison; abstract and column 8, lines 38-49 of Hendler).

As discussed above, the modified teaching of Hedden differs from the claimed invention in the preparation of said composition in enteric coated formulation. However, it would have been obvious to one of ordinary skill in the art to arrive at the instantly claimed enteric coated formulation for the purpose of the regulation of release or for the protection of the formulation since the preparation of rofecoxib, aspirin or said antioxidant in enteric coatings is old and well known in the art. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. No Claim is allowed.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

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